TABLE 17. Antiarrhythmic Medications *(Continued)*

Classification	Mechanism of Action	Individual Agents/ Examples	Effects	Use	Side Effects	Contraindications
Late sodium channel blockers	Late sodium channel blockade	Ranolazine	Shortens action potential duration and prevents calcium overload	Atrial fibrillation, ventricular arrhythmias	Dizziness, nausea, headache, constipation, hypoglycemia	Advanced liver disease, use of strong CYP3A4 inhibitors or inducers
Adenosine receptor agonists	A_1-receptor agonism	Adenosine	Slows or blocks sinoatrial and AV node conduction	Termination of SVT	Flushing, dyspnea, chest pain, hypotension, dizziness, nausea	Severe asthma, cardiac transplantation
Cardiac glycoside	Increases vagal activity	Digoxin	Slows AV node conduction	Rate control of atrial fibrillation	Nausea, vomiting, dizziness, blurry vision and yellow halos, thrombocytopenia	Advanced kidney impairment (requires dose adjustment)

AV = atrioventricular; CrCl = creatinine clearance; CYP3A4 = cytochrome P450 3A4; NYHA = New York Heart Association; QTc = corrected QT; SVT = supraventricular tachycardia; VT = ventricular tachycardia.

Ranolazine, digoxin, and adenosine are excluded from the Vaughan-Williams classification. Ranolazine is used to treat angina and decreases the risk for atrial fibrillation and ventricular arrhythmias. Digoxin is a positive inotropic agent that also increases vagal activity, leading to a lower resting heart rate. It can be used for rate control in patients with atrial fibrillation. Adenosine is used in the acute treatment of arrhythmias to interrupt AV conduction and terminate SVT. Administering adenosine can also help in determining the type of arrhythmia.

Atrial Fibrillation

Atrial fibrillation is defined by the presence of disorganized atrial activity with an irregularly irregular ventricular response on ECG (**Figure 13**). It is the most common

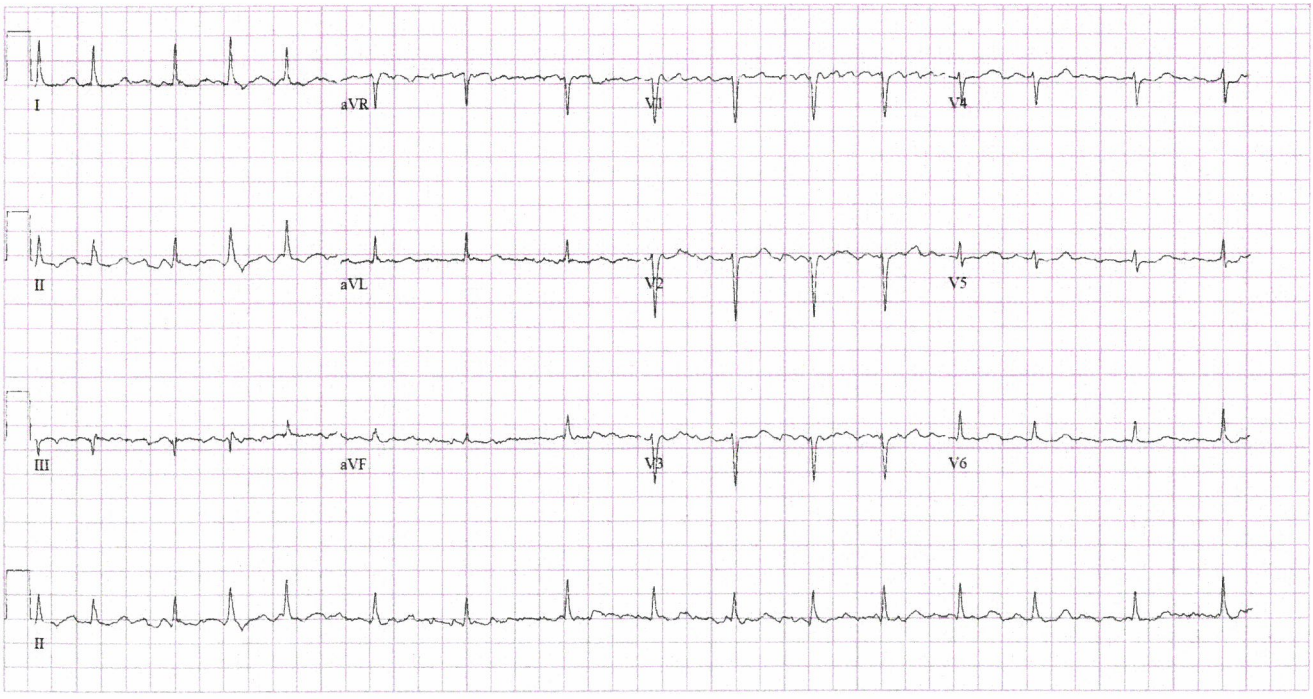

FIGURE 13. Electrocardiogram demonstrating atrial fibrillation. No clear P waves are seen, and the ventricular response is irregular.

sustained arrhythmia, affecting more than 33 million persons worldwide. Lifetime risk for atrial fibrillation is 25% in patients older than 40 years. Incidence is strongly associated with and increases with age. Accordingly, atrial fibrillation is particularly common in the elderly, occurring in 10% of persons older than 80 years. Atrial fibrillation is associated with an increased risk for adverse cardiac events, including a five-fold increased risk for stroke, as well as increased risk for heart failure and dementia. Among patients aged 55 years and older who have a cryptogenic ischemic neurologic event, such as a stroke or transient ischemic attack, occult intermittent atrial fibrillation is thought to be present in up to 25% of cases, and 30-day ambulatory ECG monitoring is indicated for detection.

Atrial fibrillation is usually the result of long-standing risk factors, such as diabetes mellitus, obesity, hypertension, coronary artery disease, heart failure, and obstructive sleep apnea. It may also be caused by reversible or acute physiologic insults, including cardiac surgery, pulmonary embolism, or hyperthyroidism. When there are no identified risk factors, a predisposing genetic background is often present.

Clinical Presentation

Patients with atrial fibrillation may be asymptomatic or experience palpitations, lightheadedness or dizziness, dyspnea, exercise intolerance, chest pain, near-syncope, or, rarely, syncope. In some cases, atrial fibrillation can lead to hemodynamic compromise, especially in patients with advanced diastolic dysfunction or restrictive cardiomyopathy. Patients with atrial fibrillation uncommonly present with tachycardia-induced cardiomyopathy, characterized by asymptomatic left ventricular dysfunction or overt heart failure.

Atrial fibrillation is categorized according to its duration. Paroxysmal atrial fibrillation stops spontaneously within 7 days of onset, whereas persistent atrial fibrillation lasts for 7 days or more. Long-standing persistent atrial fibrillation is continuous, with a duration of more than 1 year.

Acute Management

Immediate cardioversion is indicated in patients with hypotension, acute myocardial ischemia, or decompensated heart failure. R wave synchronization during cardioversion is necessary to avoid an "R-on-T" event and provocation of ventricular fibrillation (VF).

In stable patients, the primary goals of therapy are to prevent stroke, control heart rate, and minimize or eliminate symptoms. Upon diagnosis, reversible causes must be ruled out. All patients should undergo thyroid function testing to evaluate for hyperthyroidism. Patients with risk factors for or symptoms suggestive of sleep apnea should undergo testing (see MKSAP 18 Pulmonary and Critical Care Medicine). Echocardiography is indicated to evaluate for potential valvular or other structural heart disease. Echocardiography can also be used to assess left atrial size, which helps determine the severity of the underlying atrial myocardial dysfunction. Transesophageal echocardiography is often used before elective (nonemergent) cardioversion to exclude the presence of left atrial thrombus or left atrial appendage thrombus if the patient has not received adequate anticoagulation therapy (3 weeks' duration) before the procedure.

Anticoagulation

In patients who are not undergoing cardioversion, intravenous anticoagulation is usually unnecessary; however, oral anticoagulation should be initiated if the patient has sufficient risk factors for stroke. The most common method of assessing stroke risk in nonvalvular atrial fibrillation is by calculating the CHA_2DS_2-VASc score (**Table 18**). Patients with valvular atrial fibrillation (mechanical prosthesis or rheumatic mitral stenosis) require oral anticoagulation regardless of the presence or absence of other risk factors.

If cardioversion is planned, the duration of atrial fibrillation guides therapy. Patients with atrial fibrillation with a known duration of less than 48 hours have a low risk for thrombus formation and subsequent stroke, and preprocedural anticoagulation is not needed. In patients in whom the duration of atrial fibrillation is unclear or in whom atrial fibrillation has lasted longer than 48 hours, anticoagulation therapy for 3 weeks is required before cardioversion. In the absence of preprocedural anticoagulation, transesophageal echocardiography can be performed to exclude the presence of

TABLE 18. CHA_2DS_2-VASc Score, Adjusted Stroke Rates, and Antithrombotic Therapy Recommendations

CHA_2DS_2-VASc Score[a]	Incidence of Ischemic Stroke/100 Patient-Years[b]	Antithrombotic Therapy[c]
0	0.2	None
1	0.6	None or aspirin or OAC
2	2.2	OAC
3	3.2	OAC
4	4.8	OAC
5	7.2	OAC
6+	10.3	OAC

OAC = oral anticoagulation.

[a]CHA_2DS_2-VASc scoring (maximum 9 points): One point each is given for heart failure, hypertension, diabetes mellitus, vascular disease (prior myocardial infarction, peripheral artery disease, aortic plaque), female sex, and age 65 to 74 years. Two points each are given for previous stroke/transient ischemic attack/thromboembolic disease and age ≥75 years.

[b]Data from Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J. 2012;33:1500-10. [PMID: 22246443] doi:10.1093/eurheartj/ehr488

[c]Recommendations from January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al; ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014;130:e199-267. [PMID: 24682347] doi:10.1161/CIR.0000000000000041

CONT. left atrial appendage thrombus and facilitate urgent cardioversion. Regardless of the duration or nature of atrial fibrillation, all patients who undergo cardioversion must receive anticoagulation therapy for at least 4 weeks following the procedure owing to an increased risk for thromboembolic events after sinus rhythm is restored.

Cardioversion and Rate Control

Pharmacologic or electrical cardioversion should be pursued in patients with significant symptoms despite rate control. In patients without structural heart disease, class IC agents or ibutilide can be considered for pharmacologic cardioversion. Patients treated with ibutilide should be monitored on telemetry for a minimum of 6 hours or until the QTc returns to baseline, owing to a small risk for torsade de pointes.

Heart rate control is necessary in patients with rapid ventricular rates to improve cardiac function and alleviate symptoms. Acutely, the goal heart rate should be between 60/min and 110/min. Commonly used medications include AV nodal blockers, such as metoprolol or diltiazem. Intravenous or oral administration may be appropriate depending on a patient's symptoms. In patients with left ventricular dysfunction, calcium channel blockers should be avoided. Digoxin can be used as adjunctive therapy to improve rate control, especially in patients with heart failure.

Long-Term Management

Anticoagulation

Arterial thromboembolic events are the most serious complication of atrial fibrillation. In nonvalvular atrial fibrillation patients, the absolute risk for stroke is approximately 4% per year; however, the presence of comorbidities (such as heart failure, hypertension, diabetes, or vascular disease) can increase the risk 15- to 20-fold. Hypertension is associated with an increased risk for both atrial fibrillation and stroke; therefore, blood pressure control is critical in the management of atrial fibrillation.

Stroke prevention with antithrombotic therapies is dependent on the patient's risk for stroke and risk for bleeding. Although several risk stratification scores are available, current guidelines recommend the use of the CHA_2DS_2-VASc score in patients with nonvalvular atrial fibrillation. Adjusted stroke rates and recommendations for antithrombotic therapy based on the CHA_2DS_2-VASc score are shown in Table 18. Patients with nonvalvular atrial fibrillation who have a CHA_2DS_2-VASc score of 2 or higher should be treated with anticoagulation to prevent stroke. Patients with valvular atrial fibrillation (rheumatic heart disease, mitral stenosis, and valve replacement) should receive warfarin. Non-vitamin K antagonist oral anticoagulants (NOACs) are not approved for use in valvular atrial fibrillation. However, patients with atrial fibrillation and other valvular lesions (aortic valve disease, mitral regurgitation, and tricuspid regurgitation) are eligible for NOAC therapy.

Bleeding scores, such as the ATRIA, HAS-BLED, and ORBIT scores, may be used to identify patients with significant bleeding risk based on patient characteristics, including anemia, hypertension, labile INR, older age, kidney insufficiency, and treatment with antiplatelet medications. Reversible risk factors for bleeding should be addressed in patients receiving anticoagulants. Concomitant antiplatelet therapy should be avoided unless the patient has recent active coronary artery disease (acute coronary syndrome or revascularization within the past year).

Several oral anticoagulants are available for stroke prevention in patients with atrial fibrillation. Vitamin K antagonism with dose-adjusted warfarin is an effective, low-cost therapy; however, warfarin has limitations, including the need for frequent monitoring and adjustment and numerous food and drug interactions. The safety and efficacy of warfarin therapy depend on the time the patient is in the therapeutic range (INR 2-3).

Four NOACs are approved for the prevention of stroke in atrial fibrillation (**Table 19**). Dabigatran, an oral direct thrombin inhibitor, is superior to warfarin for the prevention of ischemic stroke and results in less intracranial bleeding. Patients taking dabigatran have a higher risk for gastrointestinal bleeding relative to warfarin and may experience dyspepsia. Rivaroxaban, a direct factor Xa inhibitor, is noninferior to warfarin in the prevention of stroke or systemic embolism and is associated with less intracranial and fatal bleeding. As with dabigatran, patients taking rivaroxaban have a higher risk for gastrointestinal bleeding compared with those taking warfarin. Apixaban, another oral factor Xa inhibitor, is superior to warfarin for the prevention of stroke and confers less risk for major bleeding, including intracranial bleeding. Edoxaban is noninferior to warfarin for stroke prevention and is associated with less major bleeding. All of the NOACs have shorter half-lives than warfarin; however, there are no quick, readily available serum assays to accurately determine anticoagulant activity. Reversal agents and antidotes continue to be developed for these agents. Andexanet alfa is being evaluated for reversal of factor Xa inhibition, for use in patients treated with rivaroxaban, apixaban, or edoxaban. Idarucizumab is a dabigatran-reversal agent available for emergency invasive or surgical procedures or in cases of uncontrolled or life-threatening bleeding.

Approximately 10% to 25% of patients with atrial fibrillation have contraindications to oral anticoagulation or discontinue therapy for various reasons, including bleeding events. In patients who are at moderate to high risk for stroke (CHA_2DS_2-VASc score ≥3), left atrial appendage occlusion to prevent stroke and systemic thromboembolism can be considered. Occlusion of the left atrial appendage can be achieved percutaneously with a self-expanding device that is implanted in the left atrial appendage or with surgical closure. Left atrial

TABLE 19. Anticoagulants Approved for Stroke Prevention in Atrial Fibrillation

Medication	Frequency	Type of AF	Cautions and Dosing
Warfarin (vitamin K antagonist)	Dosing adjusted to INR	Valvular[a] or nonvalvular	Avoid in pregnancy Caution with idiopathic thrombocytopenic purpura, heparin-induced thrombocytopenia, liver disease, protein C or S deficiency Many drug interactions
Dabigatran (direct thrombin inhibitor)	Twice daily	Nonvalvular	Caution with P-glycoprotein inhibitors Reduce dose with CrCl 15-30 mL/min/1.73 m^2
Rivaroxaban (factor Xa inhibitor)	Once daily	Nonvalvular	Avoid with CrCl <30 mL/min/1.73 m^2, moderate liver impairment, strong P-glycoprotein inhibitors, and strong cytochrome P-450 inducers and inhibitors Reduce dose with CrCl 30-50 mL/min/1.73 m^2
Apixaban (factor Xa inhibitor)	Twice daily	Nonvalvular	Avoid with strong P-glycoprotein inhibitors or strong cytochrome P-450 inducers and inhibitors Reduce dose with two of the following criteria: creatinine ≥1.5 mg/dL 133 (μmol/L), age ≥80 years, or weight ≤60 kg (132 lb)
Edoxaban (factor Xa inhibitor)	Once daily	Nonvalvular	Avoid with strong cytochrome P-450 inducers and inhibitors Reduce dose with CrCl 30-50 mL/min/1.73 m^2, weight ≤60 kg (132 lb), or concomitant use of verapamil or quinidine (potent P-glycoprotein inhibitors)

AF = atrial fibrillation; CrCl = creatinine clearance.

[a]Valvular atrial fibrillation refers to atrial fibrillation in the presence of a mechanical heart valve, rheumatic mitral valve disease, and/or mitral stenosis.

CONT. appendage occlusion has a lower risk for intracranial bleeding compared with dose-adjusted warfarin.

Rate Versus Rhythm Control

Studies have not demonstrated that sinus rhythm restoration is superior to rate control alone. Consequently, the decision to initiate a rate or rhythm control strategy is predominantly based on symptoms, patient age, and patient preference. Rate control can be used to manage asymptomatic patients, with a resting heart rate goal of less than 80/min. A goal of less than 110/min may be considered in select patients without left ventricular dysfunction. β-Blockers, calcium channel blockers, and digoxin can be used to control the ventricular rate in patients with atrial fibrillation. Combination therapy may be needed to adequately control heart rate. Aside from resting heart rate assessment, evaluation of the heart rate with activity, such as with a 6-minute walk test, stress test, or 24-hour ambulatory ECG monitoring, should be performed.

A rhythm control strategy can improve quality of life in patients who continue to have symptoms despite adequate rate control. Because the long-term effects of rate control are unknown, rhythm control is often pursued in younger patients (aged <50 years) with minimal symptoms. Rhythm control may require cardioversion in addition to antiarrhythmic therapy. Antiarrhythmic drug selection is guided by the patient's comorbid conditions and safety considerations. Patients with infrequent atrial fibrillation who have no structural heart disease or conduction disease often benefit from a "pill-in-the-pocket" approach. With this strategy, patients take a class IC drug (flecainide or propafenone) at the onset of an episode of atrial fibrillation. These patients should be receiving β-blocker or calcium channel blocker therapy or should take one of these medications before taking the "pill in the pocket." Pill-in-the-pocket therapy should be initiated in a monitored setting to ensure patient safety.

Nonpharmacologic Strategies

Catheter ablation with pulmonary vein isolation is an effective rhythm control therapy in patients with recurrent symptomatic atrial fibrillation despite antiarrhythmic drug therapy. Catheter ablation is most effective in patients without significant left atrial enlargement and multiple comorbid conditions. Seventy percent to 90% of patients with paroxysmal atrial fibrillation are symptom-free 1 year after the procedure; however, success rates vary. Complications include thromboembolism (0.5%-1% risk), tamponade, and vascular complications (such as insertion hematoma, pseudoaneurysm, arteriovenous fistula, and retroperitoneal bleeding). Longer-term complications, such as pulmonary vein stenosis, are uncommon.

AV node ablation is an option in patients with atrial fibrillation who have continued symptomatic tachycardia despite rate and rhythm control therapy. Therapeutic ablation of the

AV node requires implantation of a permanent pacemaker. These patients remain in atrial fibrillation and still require anticoagulation.

KEY POINTS

- Immediate cardioversion to sinus rhythm is indicated in patients with atrial fibrillation who have hypotension, acute myocardial ischemia, or decompensated heart failure, regardless of atrial fibrillation duration.
- Current guidelines recommend calculation of the CHA_2DS_2-VASc score for stroke risk stratification in patients with nonvalvular atrial fibrillation; patients with a CHA_2DS_2-VASc score of 2 or higher should be treated with oral anticoagulation to prevent stroke.
- A rhythm control strategy can improve quality of life in patients with atrial fibrillation who continue to have symptoms despite adequate heart rate control.

Atrial Flutter

Atrial flutter is an organized macro-reentrant tachycardia with discrete regular atrial activity on ECG, usually with a rate of 250/min to 300/min. Typical atrial flutter is characterized electrocardiographically by a sawtooth pattern with inverted flutter waves in leads II, III, and aVF and positive flutter waves in lead V_1 (**Figure 14**). Typical atrial flutter is the result of counterclockwise reentry around the tricuspid annulus. In atypical flutter, the circuit can travel in a clockwise direction or can occur in other locations in the right and left atria. Atypical flutter may occur after ablation or after congenital or valvular cardiac surgery.

Management of atrial flutter is similar to atrial fibrillation management; however, a rhythm control strategy is favored in atrial flutter because rate control may be difficult and often requires high doses of more than one AV nodal blocker. Catheter ablation is the definitive treatment for typical atrial flutter, owing to a very high success rate (>95%) and low complication rate. Oral anticoagulation in patients with atrial flutter is approached in the same manner as in patients with atrial fibrillation. Patients with atrial flutter and sufficient stroke risk (CHA_2DS_2-VASc score ≥2) require oral anticoagulation to prevent stroke and systemic embolism. H

KEY POINT

- Catheter ablation is the definitive treatment of typical atrial flutter, owing to a very high success rate (>95%) and low complication rate.

Supraventricular Tachycardias

Clinical Presentation

SVTs are rapid heart rhythms that arise from the atrium or require conduction through the AV node. Atrial fibrillation and atrial flutter are technically SVTs, although the term generally pertains to paroxysmal SVTs. SVTs can affect all age groups but frequently occur in younger patients. Prevalence is higher in women than in men. SVTs usually occur in the

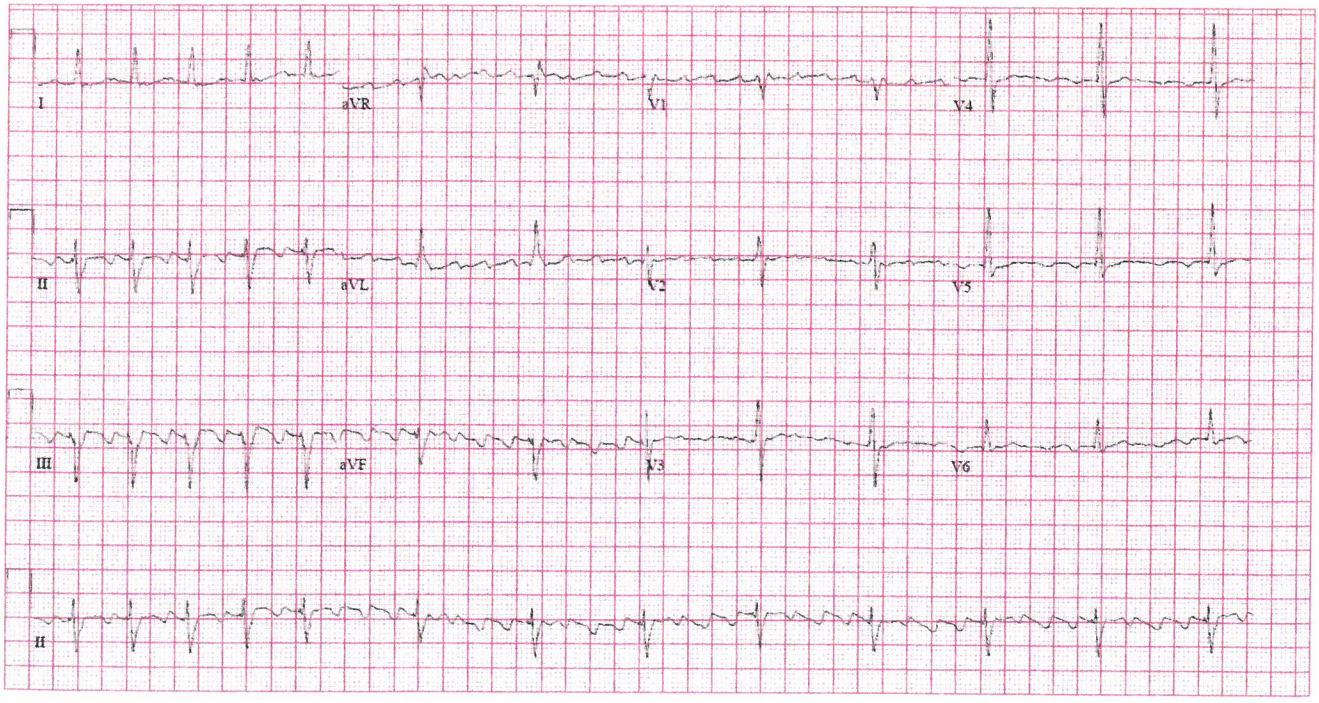

FIGURE 14. In this electrocardiogram demonstrating typical atrial flutter, negatively directed sawtooth waves are seen in the inferior leads, and positive waves are seen in lead V_1. In the bottom rhythm strip, 2:1 and 4:1 conduction patterns are seen.